

The *Next Generation* of Public Health

Delaware Public Health Laboratory (DPHL) is embarking in the new wave of identifying outbreaks and pathogens for the health of Delaware citizens. This technology is brand new with applications vastly improving current methods of testing for infectious diseases.

The technology is DNA sequencing, or the process of determining the precise order of nucleotides within a DNA molecule¹. DNA provides us with the code to the basic building blocks of all life. Each organism, from the most basic of life (bacteria) to the most complex (humans), rely on genetic information in their DNA to run routine functions, like turning oxygen into energy. Our DNA determines the color of our eyes, skin, our sex, height, predispositions to cancers, autoimmune diseases, and other biological features. This also allows scientists to determine how organisms are related, which treatments are most effective, and if these organisms came from a particular source, whether person to person or eating a contaminated food source.

In the Laboratory, when we speak about DNA, in regards to the amino acids (adenine, thymine, guanine, and cytosine) that makeup the structure of the DNA. Amino acids are called “base pairs” (bp) because they are complimentary to one another in how they pair to one another. The human genome, or the entire set of our genetic information, is approximately three billion base pairs.

DPHL has been utilizing sequencing technology for more than 10 years. We began by genotyping Norovirus, otherwise known as the stomach flu, to identify outbreaks. Following this method, we began to identify influenza virus mutations creating resistance to the antiviral therapy Tamiflu. Most recently, we have utilized DNA sequencing to identify rare and not routinely identified bacteria.

A 45 year-old male presented to a local area hospital with cellulitis stemming from cuts he received while cutting cement at his job. The patient’s cellulitis spread to his blood, causing bacteremia. The hospital isolated a small curved gram negative rod from two of the four blood cultures bottles drawn. Upon initial biochemical identification, the hospital suspected *Campylobacter*, a common food contaminant that presents as gastrointestinal disease, but can be identified in blood with those whom have compromised immune systems. The hospital submitted the organism to DPHL for confirmation. DPHL Microbiologist were unable to confirm the organism as *Campylobacter*. It did not grow on selective *Campylobacter* media. Other biochemical reactions suggested the organism as being a possible *Campylobacter* species. Using sequencing analysis, along with support from the Centers for Disease Control and Prevention (CDC), DPHL was able to identify the organism as a brand new pathogen that, as of yet, has not been given proper nomenclature. The CDC published an article in early 2016 reclassifying the organism as a new genus and species, *Haematospirillum jordaniae*³.



The sequencing technology Delaware has been using provides limited, but essential genetic information. For each sample tested, an average of 600 base pairs are sequenced. This has been incredibly beneficial for Norovirus clustering, influenza antiviral resistance, and unknown bacterial identification, but the technology is limited. If we were to sequence the human genome using those methods, it would take 6+ years⁴. In the past five years, the technology has vastly improved.



This past year, DPHL purchased, quite literally, the next generation in sequencing technology. The MiSeq, as it is named, sequences up to 80 million base pairs, or the entire genome of 16 *Salmonella* organisms. This technology will be replacing the current foodborne pathogen surveillance testing, Pulse Field Gel Electrophoresis (PFGE). In the past two summer seasons, CDC utilized whole genome sequencing (WGS) for surveillance of *Salmonella* serovar Newport, which was thought to be linked to produce sold in and around the Delmarva region. WGS is much more sensitive to identifying relationships of organisms than PFGE is capable of. This will greatly improve the way we track not only foodborne outbreaks in Delaware, but hospital acquired infections, antibiotic drug resistance, and identification of clinically significant pathogens not routinely identified due to broad defining symptoms.

Next Generation Sequencing not only has the ability to test infectious diseases, but can be used to identify noncommunicable diseases (cancer, autoimmune), forensic investigations, and even direct analysis of DNA from a direct sample¹, whether environmental or clinical. This technique is known as metagenomics. Metagenomic sequencing will allow public health officials to diagnose pathogens directly from the patient sample, without the need to harvest the organism. This would reduce time of detection, treatment, and inpatient services.

As new methods are identified, the future is bright for DNA sequencing. Delaware's Public Health Laboratory prepares to stay at the front of the pack in improving ways to identify and prevent outbreaks.

1. https://en.wikipedia.org/wiki/DNA_sequencing
2. Metagenomics - a guide from sampling to data analysis.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3351745/pdf/2042-5783-2-3.pdf>
3. *Haematospirillum jordaniae* gen. nov., sp. nov., isolated from human blood samples.
http://download.springer.com/static/pdf/698/art%253A10.1007%252Fs10482-016-0654-0.pdf?originUrl=http%3A%2F%2Flink.springer.com%2Farticle%2F10.1007%2Fs10482-016-0654-0&token2=exp=1484154492~acl=%2Fstatic%2Fpdf%2F698%2Fart%25253A10.1007%25252Fs10482-016-0654-0.pdf%3ForiginUrl%3Dhttp%253A%252F%252Flink.springer.com%252Farticle%252F10.1007%252Fs10482-016-0654-0*~hmac=8f3c7b4a44da45fd4deb704d53366588b269a841ab78f732ab0304a72339adf3
4. Sequencing Technology and Terminology. Jackson Buss, Ph.d. Harvard Medical School, Microbiology and Immunobiology